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Comparative Study of the Acquisition of Antibody to Norwalk Virus in Pediatric Populations

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Analysis by radioimmunoassay of pediatric sera from three populations showed that antibody to Norwalk virus is acquired at a significantly earlier age in a less developed and tropical area (Philippines) than in two more developed and nontropical countries (United States and Taiwan).

The prevalence of serum antibody to Norwalk virus has been reported to be between 50 and 75% among healthy adults in the United States (2, 10, 14) and in various other countries (10). In the United States (2, 10), and to a lesser extent in Yugoslavia (10), Norwalk antibody is acquired slowly in the pediatric age group, and the maximum antibody prevalence rate is not reached until adolescence in the United States. This is in contrast to the acquisition of antibody to rotavirus, another agent of viral enteritis, for which high antibody prevalence rates are reached worldwide by approximately 3 years of age (4, 7, 13). It is of interest that antibody to Norwalk virus was also acquired at an early age when a limited number of pediatric sera were studied from two other countries, Bangladesh and Equador (10).

To investigate further the rate of Norwalk antibody acquisition by children in various parts of the world, we have conducted extensive serological studies on children residing in Taipei and Manila and compared results with those obtained with children from the Boston, Massachusetts, area.

The Taiwanese sera were collected during 1975 from well children attending or born at a public health teaching and demonstration center (342 sera) (7). Additional Taiwanese specimens were acute-phase sera collected in 1975 from children with acute diarrhea seen at emergency rooms of three Taipei hospitals (51 sera) (5, 9); these patients did not seroconvert to Norwalk virus after their illness. All children were residents of Taipei and were from low to middle socioeconomic backgrounds. Sera from the Philippines were collected in 1976 from children and adults admitted to a Manila hospital (Santo Thomas University Hospital) for non-gastrointestinal disease or from infants born at that hospital (430 sera). Additional Philippine specimens were acute-phase sera from patients admitted to another Manila hospital for acute diarrhea (27 sera) (8); these patients did not seroconvert to Norwalk virus after their illness. All patients were residents of Manila and were of low to middle socioeconomic backgrounds. The 520 sera collected during 1975 to 1979 from the U.S. population (Massachusetts) are described elsewhere (2, 4). Sera were stored frozen and tested for the presence of Norwalk antibody by the radioimmunoassay blocking test previously described (2).

The age-related acquisition rate of Norwalk antibody for each of the three study populations is presented in Table 1. Antibody for the under 3-month age group presumably is maternally derived and reflects in its prevalence the antibody frequency of the adult population. In the United States, 43% of sera from the <3-month age group were positive, and 45% from the >12-year age group were positive. In the Philippines, these figures were 58 and 57% positive, respectively. After the disappearance of maternal antibody, conversion to seropositivity occurred at similarly slow rates in the United States and Taiwan. No significant differences were noted at any age group between these two populations. Norwalk antibody was acquired at a significantly faster rate in the Philippines than in the United States or Taiwan. The most significant differences between the United States and the Philippines were noted in the 3-month to 3-year ($P < 0.01$) and in the 3-year to 6-year ($P < 0.001$) age groups. It may be speculated that these varying antibody prevalence rates that were observed reflect differences in climatic and sociological conditions in the study populations. Our U.S. and Taiwan populations are located in nontropical climates. These two countries are also more highly developed than the Philippines (e.g., the per capita income in Taiwan is twice that in the Philippines) (6), and they experience lower rates of infant mortality than the Philip-

TABLE 1. *Comparative rates of acquisition of serum antibody to Norwalk virus*

Age group (yr)	Taiwan		United States		Philippines		*P* value[c]
	% Positive[a]	No. tested[b]	% Positive	No. tested	% Positive	No. tested	
0–3/12	57	28	43	70	58	26	NS[d]
3/12–3	5	254	3	81	19	59	<0.01
3–6	15	66	12	77	39	54	<0.001
6–12	24	45	27	75	43	83	<0.05
>12	NT[e]	NT	45	217	57	235	<0.05

[a] Percentage of sera tested positive for Norwalk antibody by radioimmunoassay.

[b] Total number of sera tested in each group.

[c] U.S. and Philippines populations were compared by the chi-square test. (There were no significant differences between the United States and Taiwan).

[d] NS, Not significant

[e] NT, Not tested.

pines (United States, 15; Taiwan, 18; Philippines, 59 per 1,000 live births) (6).

Norwalk virus was derived from the stool of an adult who developed a secondary case of illness during an outbreak of "winter vomiting disease" that occurred in an elementary school in 1968 (1). The virus causes enteritis in volunteers (3) and has been associated with enteritis in community-wide epidemics, family outbreaks, and waterborne and seafood-related illness and with infection among travelers with acute nonbacterial gastroenteritis (11). The importance and scope of Norwalk disease in the community has not yet been fully assessed. Investigation of this virus is hindered by the fact that it has not been cultivated in vitro; presently, either immune electron microscopy (15) or radioimmunoassay (2, 12) requiring as reagents clinical material derived from experimentally infected human volunteers must be used for studies of Norwalk virus. Serum antibody to Norwalk agent is not protective against disease (2, 16), but study of its prevalence indicates the extent of prior infection with the virus in a community. For determination of the prevalence of Norwalk disease in various populations, further studies documenting seroconversions temporally related to clinical symptoms will be required.

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LITERATURE CITED

1. **Adler, J., and R. Zickl.** 1969. Winter vomiting disease. J. Infect. Dis. **119**:668–693.
2. **Blacklow, N. R., G. Cukor, M. K. Bedigian, P. Echeverria, H. B. Greenberg, D. S. Schrieber, and J. S. Trier.** 1979. Immune response and prevalence of antibody to Norwalk enteritis virus as determined by radioimmunoassay. J. Clin. Microbiol. **10**:903–909.
3. **Blacklow, N. R., R. Dolin, D. S. Fedson, H. DuPont, R. S. Northrop, R. B. Hornick, and R. M. Chanock.** 1972. Acute infectious nonbacterial gastroenteritis: etiology and pathogenesis. Ann. Intern. Med. **76**:993–1008.
4. **Blacklow, N. R., P. Echeverria, and D. H. Smith.** 1976. Serological studies with reovirus-like enteritis agent. Infect. Immun. **13**:1563–1566.
5. **Cukor, G., M. K. Berry, and N. R. Blacklow.** 1978. Simplified radioimmunoassay for detection of human rotavirus in stools. J. Infect. Dis. **138**:906–909.
6. **Delury, G. E. (ed.).** 1979. World Almanac & book of facts 1979. Newspaper Enterprise Association Press, New York.
7. **Echeverria, P., N. R. Blacklow, M. T. Ho, G. Cukor, and R. P. Beasley.** 1977. Age distribution of antibody to reovirus-like agent in children in Taiwan. J. Pediatr. **91**:960–962.
8. **Echeverria, P., N. R. Blacklow, J. Vollet, C. V. Ulyangco, G. Cukor, V. B. Soriano, H. L. DuPont, J. H. Cross, F. Orskov, and I. Orskov.** 1978. Reovirus like agent and enterotoxigenic *Escherichia coli* infections in pediatric diarrhea in the Philippines. J. Infect. Dis. **138**:326–332.
9. **Echeverria, P., M. T. Ho, N. R. Blacklow, G. Quinnan, B. Portnoy, J. G. Olson, R. Conklin, H. L. DuPont, and J. H. Cross.** 1977. Relative importance of viruses and bacteria in the etiology of pediatric diarrhea in Taiwan. J. Infect. Dis. **136**:383–390.
10. **Greenberg, H. B., J. Valdesuso, A. Z. Kapikian, R. M. Chanock, R. G. Wyatt, W. Szmuness, J. Larrick, J. Kaplan, R. H. Gilman, and D. A. Sack.** 1979. Prevalence of antibody to the Norwalk virus in various countries. Infect. Immun. **26**:270–273.
11. **Greenberg, H. B., J. Valdesuso, R. H. Yolken, E. Gangarosa, W. Gary, R. G. Wyatt, T. Konno, H. Suzuki, R. M. Chanock, and A. Z. Kapikian.** 1979. Role of Norwalk virus in outbreaks of non-bacterial gastroenteritis. J. Infect. Dis. **139**:564–568.
12. **Greenberg, H. B., R. G. Wyatt, J. Valdesuso, A. R. Kalica, W. T. London, R. M. Chanock, and A. Z. Kapikian.** 1978. Solid-phase microtiter radioimmunoassay for detection of the Norwalk strain of acute nonbacterial epidemic gastroenteritis virus and its antibodies. J. Med. Virol. **2**:97–108.
13. **Kapikian, A. Z., W. L. Cline, J. O. Arrobio, C. D. Brandt, W. J. Rodriguez, D. A. Sack, R. M. Chanock, and R. M. Parrott.** 1976. Human reovirus-like agent as the major pathogen associated with "winter" gastroenteritis in hospitalized infants and young children. N. Engl. J. Med. **294**:965–972.
14. **Kapikian, A. Z., H. B. Greenberg, W. L. Cline, A. R. Kalica, R. G. Wyatt, H. D. James, N. L. Lloyd, R. M. Chanock, R. W. Ryder, and H. W. Kim.** 1978. Prevalence of antibody to the Norwalk agent by a newly developed immune adherence hemagglutination assay. J. Med. Virol. **2**:281–294.
15. **Kapikian, A. Z., R. G. Wyatt, R. Dolin, T. S. Thornhill, A. R. Kalica, and R. M. Chanock.** 1972. Visualization by immune electron microscopy of a 27-nm particle associated with acute infectious nonbacterial gastroenteritis. J. Virol. **10**:1075–1081.
16. **Parrino, T. A., D. S. Schreiber, J. S. Trier, A. Z. Kapikian, and N. R. Blacklow.** 1977. Clinical immunity in acute gastroenteritis caused by Norwalk agent. N. Engl. J. Med. **297**:86–89.